

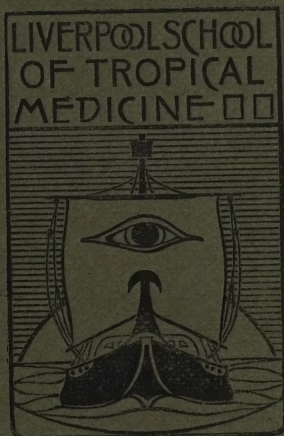
The Nature and Control of Yellow Fever

(Read at the XV International Congress on Hygiene and Demography, Washington,
September 25, 1912)

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BY
HARALD SEIDELIN

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THE NATURE AND CONTROL OF YELLOW FEVER

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BY HARALD SEIDELIN.

Yellow fever is an infectious disease, produced by *Paraplasma flavigenum* and transmitted by *S. fasciata*. The latter statement has met with universal acceptance, and we may, at present, take its correctness for granted. But it is worth while to examine the rather elaborate structure which has been erected on this foundation. The theory, as it now stands, embraces the following particulars: yellow fever is transmitted by *S. fasciata*, and by no other means, in particular by no other mosquito. The transmission can only take place after the yellow fever parasite has undergone a development in the mosquito, the duration of which is, approximately, twelve days. Yellow fever blood is infectious during the first part of the disease, but not after the third day. Transmission is believed to take place at night time only. Hereditary transmission of the yellow fever germ from mosquitos to their offspring, and infection of one mosquito from another, without the intervention of a human host, are generally considered as unproved possibilities. Each of these points must be discussed separately.

I may state at once that conclusions on these secondary points have not been drawn by the U.S. Army Commission; Reed and his fellow-workers were very careful in their statements; but the assertions of later, less-cautious, observers have so often been repeated that they are now almost universally believed.

The axiom that yellow fever is transmitted by no other mosquito than *S. fasciata* is an assertion entirely without proof; it is, nevertheless, repeated in most text-books, and even in special literature dealing with yellow fever. The conclusion drawn by a recent author (Doerr), not himself a worker on yellow fever, that the yellow fever virus must be intimately adapted to a certain mosquito-species, as experi-

ments with other mosquitos, even near-standing species, as *Culex fatigans*, have proved negative is very curious, when it is remembered how few experiments have been made, and that no experiments have ever been published with species of *Stegomyia* other than *S. fasciata*. In the study of sleeping sickness hundreds of experiments have been made to one on yellow fever, and it was until a short time ago considered an established fact that *Glossina palpalis* was the only fly capable of transmitting the pathogenic trypanosome; after many years of intense study, it came as a surprise that *G. morsitans*, and perhaps other species of *Glossina*, could transmit not only *T. rhodesiense*, but also the well-known *T. gambiense*. In other trypanosome infections, in malaria, and in Babesia infections, we know that insects belonging to different species, even to different genera, may serve as transmitters. We should be careful in drawing conclusions in the case of yellow fever, with the very scarce material at hand.

That yellow fever is transmitted in nature by no other means than by mosquitos has never been proved, but is extremely probable in view of our knowledge of protozoal diseases.

The yellow fever germ is supposed to undergo a development in the mosquito of twelve days' duration. This is made probable by the negative results of experiments in which a period of less than twelve days had elapsed after the mosquito had sucked blood from an infected patient, until it was allowed to bite a non-immune individual. This theory corresponds well with the observations of Carter and others on the extrinsic incubation period, and is likely to be correct, but cannot be considered conclusively proved, as the negative experiments referred to were not numerous, and, on the other hand, there is a comparatively large number of negative results in cases, in which all conditions for obtaining positive results were fulfilled.

Yellow fever blood is considered infectious during the first three days of the disease only, but on very scanty evidence, as I have previously pointed out. My argument

has been objected to, but not shown to be erroneous, and I must again assert emphatically that we here have to do with a theory which is without adequate foundation. The negative experiments of the Army Commission prove nothing in this respect. In Carroll's table of twenty-two cases, with *thirty-two* negative inoculations, we find *two* inoculations only in which the patient bitten was in a later period than the third day, whilst the interval allowed in the mosquito was more than twelve days (thirteen and fourteen respectively). In ten inoculations both conditions for favourable results were fulfilled (patient bitten during first three days of disease, and intervening period in mosquito twelve days or more). In the remaining twenty inoculations the interval in the mosquito was less than twelve days, which circumstance alone would explain the negative result. It really surprises me that anybody can take this table as an argument in favour of the three days' infectiousness.

The responsibility for this dogma rests with Marchoux and Simond, and theirs should be the honour for having enunciated it, should it finally prove to be correct, but proved it they have not. I have in a former paper analysed the four experiments which sustain their argument, and shall not go into details here. All four experiments are with infection of blood or filtered serum, and in one only was the infected individual proved, by subsequent mosquito inoculation, susceptible to yellow fever. The experiments are, therefore, both very few and of very relative value. Never has a dogma in medicine been established on evidence poorer than this.

Transmission of yellow fever is said to take place only during the night. This doctrine is supported by a considerable amount of epidemiological evidence, mostly from the pre-mosquito period. The general knowledge of *S. fasciata's* biology did not seem at first to answer the epidemiological experience, as it is almost universally recognized that *S. fasciata* bites indifferently at day and at night, or it is simply called, by several authors, a day-mosquito, thus differentiating it from the typical night-

mosquitos. The apparent contradiction between these experiences has, however, been explained by Marchoux and Simond, who found that only young females, which suck blood for the first time and have consequently no chance of being previously infected, bite at daytime, whilst the older, and possibly infected females have learnt cautiousness and remain hidden during the day, to sally forth to attack in the darkness. If this holds good, the old observation need not surprise us, but I do not think the question can be looked upon as finally settled; severe mistakes might occasionally occur, if non-immunes were taught that they could, during the day, visit yellow fever infected places with absolute safety. The matter is evidently of very great practical importance for foreigners, residents and visitors in yellow fever countries.

Hereditary transmission in mosquitos and infection of mosquitos by feeding on sugar-water containing triturated, infected mosquitos, have been observed by Marchoux and Simond, in one experiment of each kind. The latter mode of transmission would probably be of quite exceptional occurrence in nature, but the former might explain some obscure epidemiological facts, especially the apparently spontaneous, isolated outbreaks in sparsely populated countries.

With regard to the pathogenic organism in yellow fever I shall not discuss earlier investigations, as I have done so in another paper. I shall only refer to my own investigations, which were commenced in 1908; in 1909 I published a preliminary note, and later on more detailed accounts. The limited time at my disposal does not allow me to discuss particulars, but I would briefly refer to the results obtained on the Expedition to Yucatán for the Liverpool School of Tropical Medicine, from which I have just returned; the detailed report of this Expedition will appear in a few weeks.*

The parasite which I have described, and for which I have proposed the name of *Paraplasma flavigenum*, has been

* *T. F. Bur. Bull.*, Liverpool, Oct., 1912, II, 2, pp. 123-242.

found by me in earlier researches in over ninety cases of yellow fever out of a little more than a hundred cases examined, and, in the last series, in sixteen cases out of seventeen cases officially diagnosed, clinically or post mortem, in which the blood was examined. Moreover, *P. flavigenum* was found in twenty-one cases, not officially confirmed as yellow fever but many of them clinically very much suspected of being so, and in none could this diagnosis be excluded. The diagnoses given in these cases were mostly gastric fever, bilious fever, or similar ones. Finally, the same intracorpuseular parasite-like bodies were observed in two apparently healthy native children; these two cases, together with two similar ones which I have observed during my earlier investigations, may represent very mild infections, or the individuals may be chronic parasite carriers. A very large control material, consisting of over four hundred cases, mostly of febrile diseases, as malaria, typhoid fever, etc., were carefully examined with negative results.

P. flavigenum has been observed from the first to the fourteenth day of the disease. There is no reason, however, to consider fourteen days as a general time limit for its presence, as the corresponding case was a very prolonged one, with a pronounced recrudescence after five or six days. That the parasite has been found on the tenth day, in a very mild case, represents relatively a later stage of the disease.

The parasite is morphologically polymorphic. The forms most commonly observed are small and intracorpuseular, consisting of one or two chromatin granules, and a more or less well-defined, protoplasmic body. The largest intracorpuseular elements have been seen in smears from liver and spleen. Free elements have been seen, both in smears and in organs. Some of these are comparatively very large, and show considerable resemblance to the gametocytes of the protozoal blood-parasites.

Many of the intracorpuseular elements are not unlike forms of *Babesia*, others are more like *Theileria*, and others again like *Anaplasma*. It has, therefore, been proposed to establish a new genus, *Paraplasma*, in the family *Babesiidae*.

The parasites stain, with some slight difficulty, with Giemsa's stain, and with other modifications of Romanowsky's method; but, in all cases, staining should take place for a somewhat longer time than in the case of malarial parasites. It was an agreeable surprise that good results were obtained with Giemsa's quick method, prolonging the action of the undiluted stain to one minute, and of the diluted to ten minutes, instead of half a minute and five minutes respectively. Satisfactory results have also been obtained with various haematoxylin methods, especially with Delafield's solution and with Heidenhain's iron-haematoxylin, as well as with my own iron-haematein technique. The latter group of methods are particularly useful in staining sections, but are also of use in checking the results obtained with the Romanowsky method; there is at present a tendency to regard Giemsa's and other azur-eosin stains as particularly unreliable, a somewhat exaggerated tendency, I believe, but, of course, it is always a safeguard to use several methods.

Before we discuss the measures to be taken against yellow fever, a few words should be said with regard to its epidemiology.

It was believed when it was found out that yellow fever is transmitted by mosquitos, that it would only be a question of a few years to stamp it out. Now this has not been the case. It is not the place here to enquire in detail why it has not been possible, but it appears that the success of the campaign in some places, and its failure in others, have supplied a remarkable proof of the correctness of the mosquito theory; mosquito extermination has been comparatively easy in large cities and in limited districts under the direct control of a powerful government, and it is in such places only, as Habana, New Orleans, Panama Canal Zone, Rio de Janeiro, and Vera Cruz that really demonstrative results have been obtained. Not in all of these places has the number of mosquitos been kept continually at a very low level; in Habana I have been informed that mosquitos, including *Stegomyia fasciata*, have lately become more

common than in previous years, and some authorities have told me that they were not at all uncommon in the Canal Zone. This should not be so; careful vigilance should be maintained, as long as there is any possibility of re-introduction of infection. This possibility not only exists, but is abundantly present. We should be cautious and not feel secure too early; the history of epidemics teaches the lesson, that the great infectious diseases are subject to oscillations, on which even the most radical measures have little influence.

To give an idea of the actual prevalence of yellow fever, I shall only mention that 716 deaths were officially reported in 1910, and 488 in 1911; in the first six months of 1912, there have already been about 500 deaths. There is little doubt that these figures represent a minimum.

One of the most important points in the epidemiology of yellow fever is the existence of unrecognized, and unrecognizable cases. It is the experience of nearly all observers that yellow fever may present all degrees of intensity from severe, fatal cases, to mild, atypical attacks of very short duration.

Cases belonging to the second group are not uncommon; their importance for epidemiological questions is obvious. It is asserted by both ancient and modern observers that the susceptibility of an individual diminished with the length of time during which he has resided in a yellow fever infected country. This phenomenon we are entirely unable to explain, if we do not admit that the (relative or absolute) immunity has developed as a consequence of acquired infection.

This matter is very clear, and will be universally agreed to, I believe, as long as we deal with foreigners. But when the same consideration is extended to natives, as it has been done by Marchoux and Simond, Otto, Boyce, and others, opposition is often met with. Nothing, however, can be more clear; if an individual is immune to yellow fever, it is reasonable to conclude that he has already gone through at least one attack of the disease.

When the immunity is considered in this way, we can form a definite idea of epidemiology. Yellow fever is endemic in certain areas, at present in several parts of México, Brazil, Central America and Ecuador, and, in the old world, in West Africa. The infection is continuously maintained, in a mild form, in those countries, but tends to give rise to epidemic outbreaks, on some occasion or other, for instance the arrival of a considerable number of non-immune foreigners. In the meantime, between outbreaks, the infection is continued in natives who are infected in childhood and, therefore, not liable to typical attacks later on. Most cases in native children are atypical, and many are mild; they are consequently not recognized, but nevertheless confer a certain degree of immunity. Later in life, these individuals will continually be exposed to mosquito bites, and probably be bitten many times by infected *S. fasciata*. They will not, however, develop yellow fever, but either present no symptoms at all, or only those of a mild febrile disorder. In the former case, we would have to speak of microbe carriers, in the latter simply of mild infections. It is very likely that microbe carriers exist, but we have no idea, for how long a time parasites may remain living in their blood. Minchin advocates the view that the existence of microbe carriers, i.e., symbiosis, demonstrates a higher degree of adaptation to the host than an infection which does harm to, or even kills, the host. In yellow fever, a very well advanced stage of adaptation seems to exist; thus, we may expect to find chronic carriers of yellow fever microbes.

This hypothesis goes a long way to explain many epidemiological facts, which remain obscure at present, especially the occurrence of repeated but separate outbreaks in sparsely populated areas (Sudan), where not even the existence of unrecognized cases with mistaken diagnosis would furnish a sufficient explanation of the persistence of the virus in the area.

Severe, even fatal cases of yellow fever are occasionally observed in natives in endemically infected countries. The

apparent contradiction between this experience and the ordinary immunity of natives may probably be explained in the following way: the large majority of natives in all places of an endemically infected country, and in populated centres practically all natives, have for centuries become infected with yellow fever virus, each individual repeatedly, even frequently, during his lifetime. Thus a continuous supply of virus is kept up, and all individuals are continually exposed to infection. In the case of foreigners arriving at such a place, the result is that all are inoculated with the germ, and a certain percentage taken ill with typical symptoms, whilst others develop mild, unrecognized infections, and others again are quite slowly vaccinated without ever presenting pathological symptoms—briefly we have similar differences in susceptibility as in other infectious diseases. In the natives, conditions are different: they are all infected in childhood, and in this case two circumstances may concur to modify the result of an inoculation. Firstly, cases of yellow fever in childhood are often quite different from those observed in adults, a circumstance which may not influence the prognosis, but causes the disease to be called by other names. Secondly, a certain degree of immunity may have been transmitted hereditarily, antibodies having passed from mother to child; this factor would influence both prognosis and diagnosis. A few cases in native children might be both typical and fatal even in large, severely infected cities—but to the rule that all children become inoculated there would be no exception. Therefore, there are no cases of severe yellow fever in adult natives in infected cities. In country districts conditions are somewhat different. Not only the number of human hosts is less, but in many cases also that of mosquito-hosts, other mosquitos taking to a certain extent the place of *S. fasciata*. Thus, it may happen in a district that the virus dies out, and, if communication is scarce, and especially, if people never spend the night—the most dangerous time for infection—away from their districts, then a generation may grow up, the members of which have not acquired immunity

and have soon lost their hereditary immunity. If the virus is re-introduced into such a community, infection will spread and kill as it is apt to do in a country where *S. fasciata* prevails, but which has hitherto been exempt from infection.

So much for epidemiological conditions; I have expressed myself in general terms, not discussing the particular outbreak which I have just recently observed in Yucatán; for all details I must refer to my report.

It is evident that, if so many varieties of yellow fever exist, the diagnosis must be one of extreme difficulty. And nothing can be more important for a successful campaign against yellow fever—in exposed and recently infected areas—than an early and indisputable diagnosis. A few observers (Guiteras and Lebrede) maintain that an indisputable, if not early, diagnosis can be made in all cases of yellow fever, but most authors, as well as most experienced practitioners whom I have met with, regard this as an impossibility. Not a single symptom is constant, nor pathognomonic. The relative intensity of the symptoms varies considerably. One cannot lay too much stress on a careful clinical examination, but I must emphasize that I now consider an examination of the blood necessary, not only to exclude a diagnosis of malaria, but also to demonstrate the existence of the yellow fever germ. Malaria cannot always be excluded because of the absence of malarial parasites, namely, if quinine has been taken, and on the other hand, the presence of *Plasmodium* does not exclude the diagnosis of yellow fever, as the two diseases may well exist at the same time. The demonstration of *P. flavigenum* has in several cases enabled me to make a diagnosis of yellow fever before seeing the patient, and the diagnosis has afterwards been confirmed clinically. The demonstration of *P. flavigenum* is difficult; a very thorough examination of well prepared and intensely stained blood smears is necessary, and the best microscopic outfit is none too good. It is almost useless to work with an ordinary 1/12" immersion lens; truly, I have often seen the parasites with such a lens, when I was aware of their existence and had

localized them before, but for the detection of *Paraplasma* I consider an apochromatic immersion lens and compensating oculars, a necessity. The examination should be repeated, if a negative result is obtained, and the case continues suspicious. My belief is that this means of diagnosis will become as essential in yellow fever as is the bacteriological examination in plague and cholera.

Prophylactic measures may be divided into two groups, one dealing with the protection of mosquitos against acquiring infection from human individuals, and the other with the protection of non-immunes against the bites of infected mosquitos. The former group includes detection of infected individuals and their isolation, the second segregation and mosquito protection. Mosquito destroying measures are common to both groups, and may be first considered.

We destroy mosquitos by killing larvae or impeding the laying of eggs, and by killing adult mosquitos. For the former purpose we have to abolish unnecessary water containers and to screen or oil such containers which cannot be dispensed with, or, in some cases, to stock them with larva-eating fish. I have failed to see the advantage of substituting the use of chemical poisons dissolving in water for the generally accepted method of spreading petroleum on the surface of the water; the latter method seems to me the least objectionable. It is unnecessary to enter into a detailed discussion of larva-destroying measures; those in general use are efficient if carried out thoroughly. Unfortunately the position regarding the destruction of adult mosquitos is not so well defined. So far fumigation with sulphur is the method in general use; it is an efficient and comparatively cheap method, but the disagreeable smell and the damage done to metals, fruit and vegetables is a serious drawback.

The Nocht-Giemsa method, disinfection with CO, which is recommended for the destruction of rats, is said by the inventors to be inefficient against mosquitos. I have, however, found light-gas to be a powerful culicide in

laboratory experiments, but have, so far, made only a few experiments on a larger scale of which the result seems to be that it is quite feasible to obtain very good results in this way. The action of the gas must be somewhat more prolonged than that of the sulphur dioxide, but the cost was not considerably higher, not even in Yucatán, where gas is very expensive. As far as I can judge, the recently published fumigation with cresyl (Bouet and Roubaud) would seem even more efficient and cheaper than both the sulphur and the gas methods, without possessing serious inconveniences, and I am, therefore, at present engaged in a study of its practical application. The pyrethrum method is not quite reliable, as the mosquitos become stupified only, but are not killed, and cyanide and phenol-camphor are somewhat expensive.

The measures which have for their object to impede mosquitos of gaining access to infected individuals, namely, early detection of cases and their isolation, are of the utmost importance as protection measures against the introduction of yellow fever into non-infected places in which *S. fasciata* are present, but of much less importance in endemically infected areas. They make it necessary to carry out a careful inspection of all passengers arriving from infected places and their observation during the possible incubation period, either in quarantine or by daily inspection (the so-called surveillance, or vigilance system).

The protection of non-immunes against the bites of infected mosquitos must practically consist in their thorough protection against mosquito bites in general, at any rate during night-time, as it is the only safe plan in endemic areas to regard all *Stegomyia* as infected, and a very high percentage of mosquitos are *Stegomyia*, which occur together with other mosquitos. Segregation—living at a distance from the native quarters—can, of course, in some places be useful to a certain extent, but it is by no means an efficient measure. And to pass one's whole time in a screened house, or, at any rate, each night from four or five o'clock in the afternoon to eight in the morning, is a way of living which will soon become

insupportable to most people. Therefore, protection of non-immunes in endemic areas is theoretically a very valuable measure, but practically it is always carried out in a very imperfect way, and cannot be relied upon.

In order to put matters clear and on a basis for discussion, I shall now briefly sum up the measures which I think should be put in force, in each of the following three cases:—

Endemic areas, exposed places and epidemics in places where yellow fever is ordinarily absent.

Endemically infected places. In these places all stress should be laid on the eradication of mosquitos, and, as the destruction of adult mosquitos on a large scale in a whole city is utterly impracticable, it follows that all available energy should be directed towards the destruction of larvae or towards the prevention of mosquitos depositing their eggs.

With this object in view, all water collections should be abolished, whenever possible, and those which cannot be dispensed with, screened or covered with oil at least once every ten days, but better still once a week. The oil being calculated at the rate of about two ounces to the square superficial yard (about 60 c.c. to the square metre). All kinds of petroleum may be used; the best is probably a mixture of about two parts of refined petroleum to one part of the crude oil. This layer of oil will prevent the female mosquitos from depositing their eggs on the surface of the water, and, which is more important, will kill larvae and pupae by suffocation. The latter is the most important because it will always occur, even if the oil disappears in the course of one or several days through evaporation and because of disturbance by the wind and movements of the water. Thus it may happen that eggs are deposited on the water and start developing, but they will never finish it before the next oiling takes place, as the minimum of evolution from egg to imago is, even under favourable circumstances, more than ten days. On the other hand, all larvae will perish if the oil-layer remains continuous for at least six or eight hours, and nearly all if it remains so only for one or two hours.

Larvae-eating fish should be stocked in water kept for ornamental purposes.

No measures need be taken in the case of running water, but it cannot be taken for granted that mosquito larvae do not thrive in water because it is frequently moved, if it is, on the other hand, left stagnant for a considerable length of time. Thus, larvae have been found in wells from which water was extracted several times a day with a bucket. Also containers which are said to be emptied daily should be looked upon as suspicious; they frequently contain larvae, which go to the bottom when the container is emptied and remain living in a very small quantity of water until the container is filled again.

These measures can be made obligatory for householders, and be enforced by fines, or they can be carried out by the health authorities; the latter is, I believe, the better plan.

In either case frequent inspections are necessary in order to make sure of the absence of forbidden collections of water, and that oiling and screening are properly carried out; in the case of cesspits it must be remembered that mosquitos may enter and escape through a pipe outlet, even if of a length of several metres.

These are the principal measures in endemic areas, and should, if faithfully carried out, lead to the complete eradication of mosquitos. Additional measures may be useful, as the detection of cases, their isolation, and fumigation of infected houses; but their importance cannot be very great, considering that for each case of typical yellow fever which always occurs in a foreigner, there are probably tens, and very likely hundreds, of cases, mostly in natives, which are never detected. Therefore, if the funds available are not unlimited, as they seldom are, it will be more useful to employ all the forces to destroy mosquitos, and simply exact from practitioners reports of all suspicious cases, instead of keeping up a costly system of inspectors to visit the residences of foreigners and occasionally detect a case on the third or fourth day of yellow fever, sometimes later, very seldom before, and often not at all.

Exposed places should also rid themselves of mosquitos so that there would be no danger of spreading should a case of yellow fever happen to be introduced. An exposed place is one where *S. fasciata* is present, and the risk incurred by the introduction of yellow fever cases increases proportionately to the prevalence of *Stegomyia*. If these mosquitos are completely exterminated the place ceases to be exposed to infection, and there need be no measures against the import of cases. But as long as this is not attained, the greatest possible care should be taken to avoid introduction of individuals suffering from yellow fever. And in all places where the conditions of temperature are favourable for *S. fasciata*, the importation of mosquitos should be prevented by all means.

Anti-mosquito quarantine consists in careful fumigation of all ships arriving from infected or suspected ports, unless it can be reasonably proved that a ship has not been exposed to the introduction of mosquitos on board in such a port. As proof of this, a certificate might be accepted stating that the ship has remained moored during the whole of its stay at a safe distance, i.e., from 200 to 500 metres, according to the conditions of the harbour, whether open and exposed to wind or closed. For loading and unloading, mosquito-proof lighters must have been employed. In the case of screened ships it should form no objection that they had been close to the shore, or even at a pier, in order to take passengers on board, if all non-screened departments, particularly the holds, have been kept carefully closed during that time.

Fumigation should include all parts of the ship; under no conditions should the holds be exempted, particularly in fruit ships, which are more likely to harbour mosquitos than any other.

With regard to passengers, they should pass an initial examination, state their point of destination, and sign a declaration that they will report to the local health officer twice daily for two weeks. In the event of any suspicious sign, they would be immediately isolated. Passengers

arriving in mosquito-proof ships, but not in other ships, might have the number of days since the departure from an infected port discounted from the total of fourteen.

Several authorities maintain that this observation of passengers is insufficient, and advocate the real quarantine system. But when it is considered that Germany, with a large land frontier and immense traffic has been able to protect herself against importation of cholera from Russia for years, it seems strange that more stringent measures should be necessary in the case of the comparatively limited maritime traffic from yellow fever places to neighbouring ports. Another point of importance is also that it presents little difficulty to extend the observation period to a fortnight instead of six days, but it would be nearly impossible to establish a quarantine of fourteen days which must be considered necessary in view of the experience of Marchoux and Simond, that a natural incubation period of thirteen days is occasionally observed.

An additional, very important, advantage is that this system can easily be applied to all passengers—immunes and non-immunes. Health authorities are thus saved the discussion of doubtful cases of immunity, and the possibility of repeated infections is taken into account.

Thus, mosquito-proof ships should have their screened departments exempted from fumigation, and their passengers should be allowed a shorter observation period corresponding to the duration of the voyage; other ships should be completely fumigated and their passengers complete the whole period of observation. A careful mosquito inspection should always be made on screened ships before any exemption is conceded.

In the case of an *epidemic outbreak* in a non-endemic area the importance of measures is inverted as compared with the conditions in endemic areas. Larvae destruction and prevention of mosquito breeding take a secondary place, as their effect would not be felt until after several months; detection of cases, isolation, and fumigation of infected houses, on the other hand, become the principal measures.

Finally, a small number of non-immunes on *expeditions* and in similar cases should protect themselves as far as possible by segregation and screening.

I believe that the individualising methods here advocated would be more efficient and cheaper, as well as less oppressive, than the combined and often more stringent methods which are in use in some places.

There is no time left to discuss classification of ships. I shall only say that, in my opinion, there is no reason to distinguish between infected and suspected ships. A ship with yellow fever cases on board constitutes no danger if there are no mosquitos on board; in this case no disinfection is necessary, but passengers should be looked after as mentioned. On the other hand, a ship carrying mosquitos, but with no yellow fever cases, may be extremely dangerous. It is unjustifiable to declare a ship harmless after twenty days (extrinsic and intrinsic incubation), as there is no guarantee that mosquitos would always infect individuals on board, instead of remaining in the holds during the passage and escaping on arrival.



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